

# PFO Closure for Secondary Prevention of Paradoxical Embolic Stroke: Randomized Trial Synthesis

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# Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest, arrangement, or affiliation with the organization(s) listed below:

Affiliation/Financial Relationship

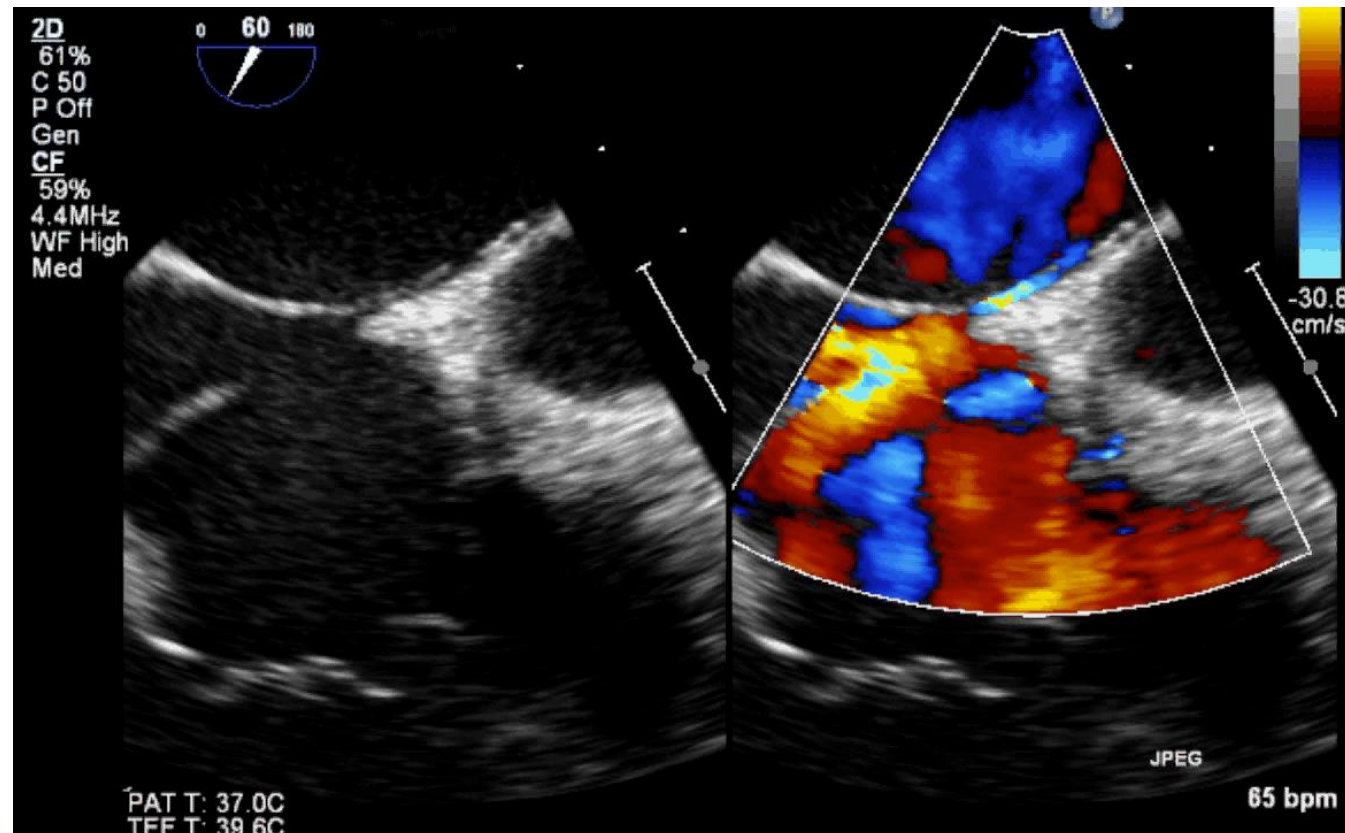
Company

Consulting Fees/Honoraria

Abbott, Edwards Lifesciences

# New Years Eve 2013

- 14y/o girl admitted with large stroke → successful iv lysis
- 2d later: herniation → emergent craniotomy → † 1d later



# In memoriam



Ariel Sharon (Scheinermann)  
1928-2014

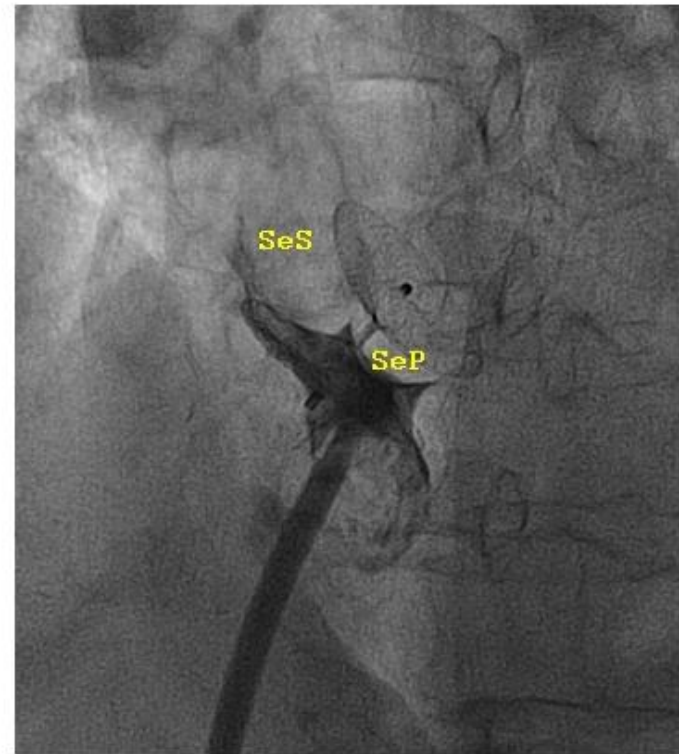
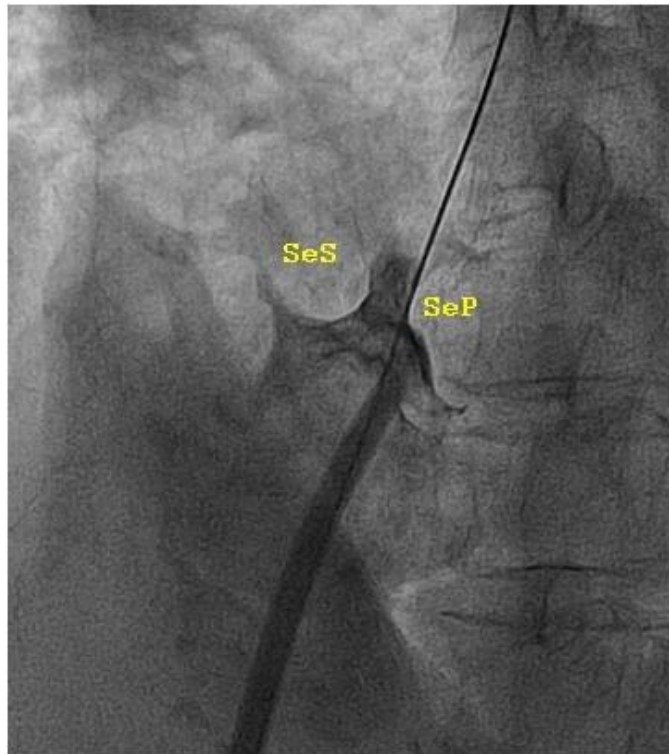
Coma after cerebral hemorrhage  
2006-2014

January 11, 2014

- **Dec 18, 2005:**A. Sharon (78y, prime minister of Israel), suddenly difficulties articulating
- Diagnosed with a transient ischemic attack (TIA); recovered quickly.
- Slated to undergo percutaneous PFO closure after the Holidays on January 5, 2006.
- Bridged to PFO closure with low-molecular weight heparin.
- **Jan 4 2006** collapsed at home d/t hemorrhagic stroke.
- Remained in a coma for 8 years, until his death in **January 2014**.

# PFO causes stroke, PFO kills


- Simple therapy: local anaesthesia, outpatient procedure, 15'



# 6 RCT's

- CLOSURE I (Furlan, NEJM 2012) → 'negative'
- PC Trial (Meier, NEJM 2013) → ,negative'
- RESPECT (Carroll, NEJM 2013) → ,negative'
- CLOSE (Mas, NEJM 2017) → ,positive'
- REDUCE (Sondergaard, NEJM 2017) → ,positive'
  
- DEFENSE-PFO (Lee, JACC 2018) → ,positive'

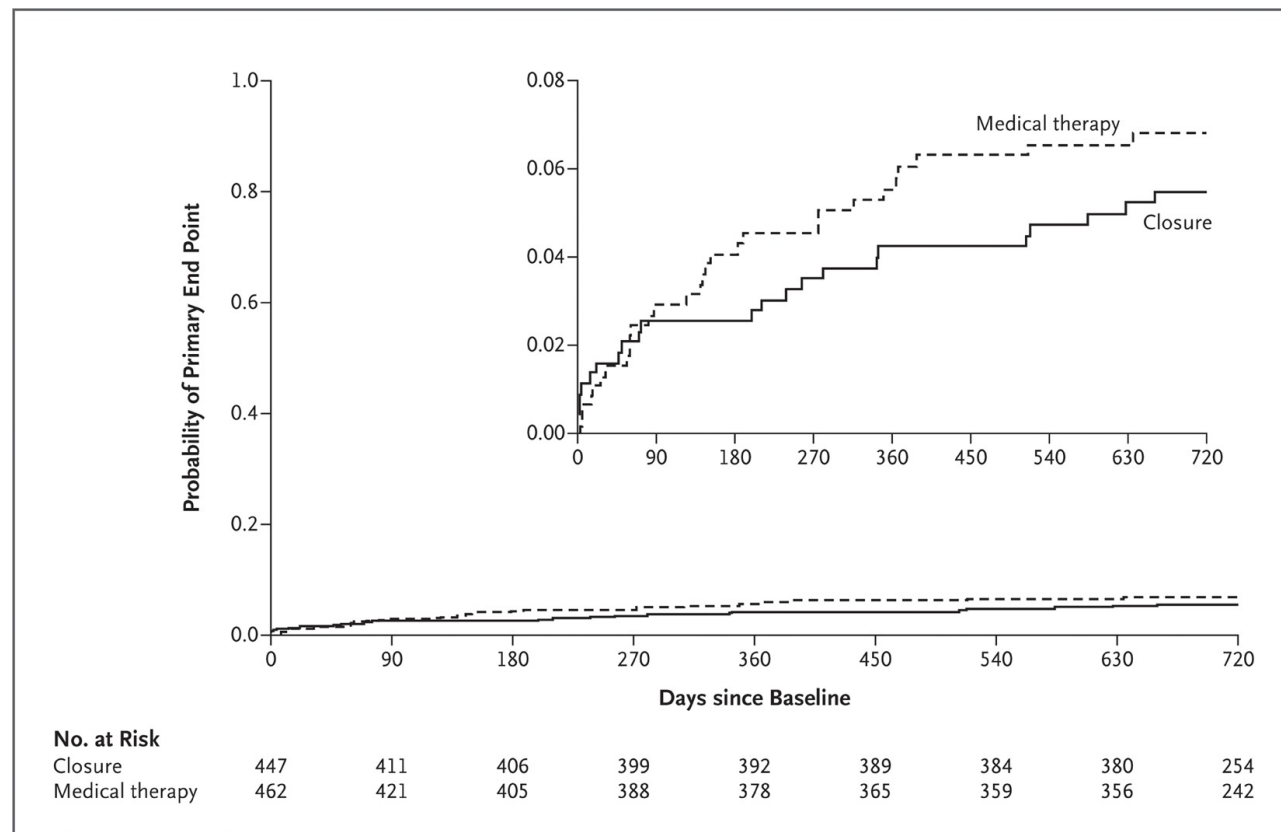
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- 
- PFOO, accepted'

# Initial PFO trials: truly ,negative‘?

- CLOSURE I:

- STARFlex
- 1. EP: Death, stroke, TIA
- (Non)-CLOSURE I
  - Procedural success: 89% (?)
  - Closure rate: 86%
- Devicethrombus: 1.1%
  - Causing stroke in 2pts
- AF in 5.7%, relevant in 1.5%

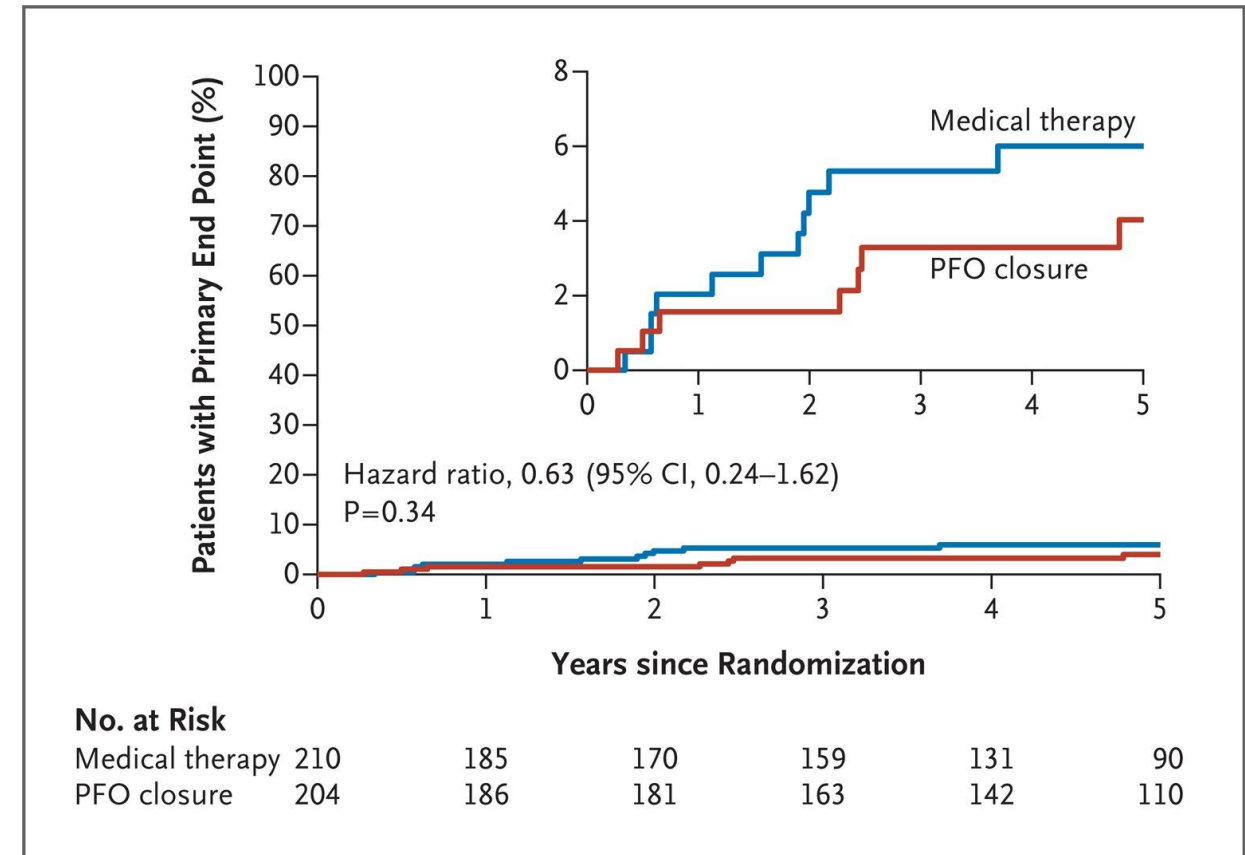




# Initial PFO trials: truly 'negative'?

- PC:

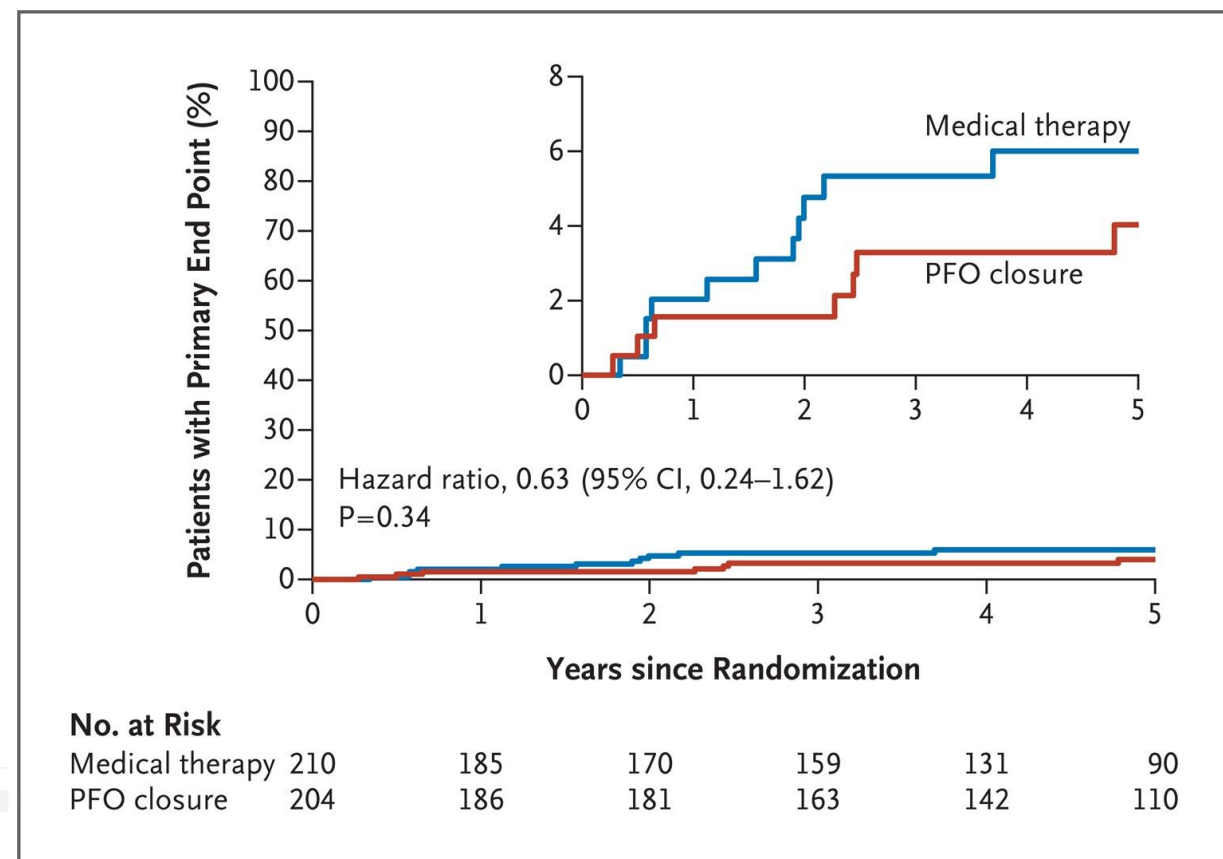
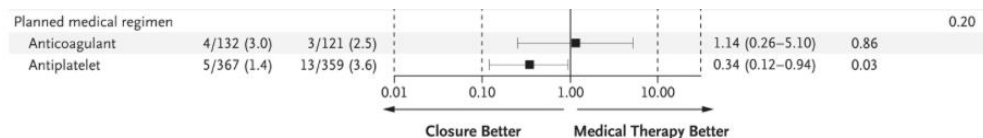
- Amplatzer
- 1. EP: Death, stroke, TIA
- Procedural success: 96%
  - Closure rate: 96%
- Stroke: 0.5% vs 2.4% (p=0.14)
  - Cross-over to PFOO 2 out of 5pts
- AF in 2.9%, relevant in 1.5%



# Initial PFO trials: truly ,negative‘?

- RESPECT:

- Amplatzer
- 1. EP: Death, stroke, TIA
- Procedural success: 96%
  - Closure rate: 94%
- 1. EP: 9pts vs 16pts (p=0.08)
  - As treated: 5 vs 16pts (p=0.007)
- AF in 3%

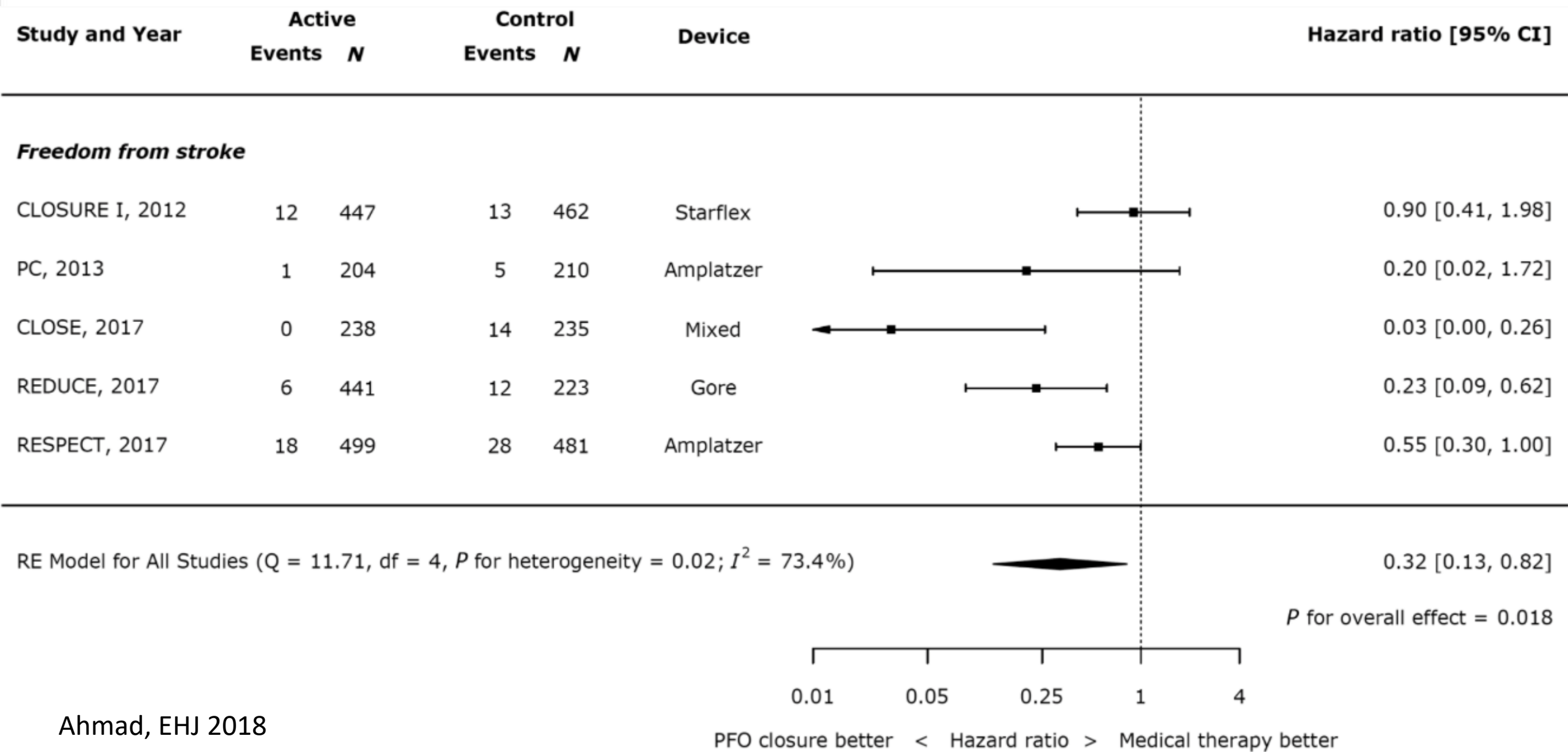


# Lessons learned from initial PFO trials

- No trial showed harm of PFOO (adverse events)
- Numerically PFOO always superior
  - Underpowered?
  - Not long enough F/U?
- Subgroup analysis
- As-treated/PP analysis

 Many hints that PFOO may indeed be better → still: not accepted by many

**What do we do, when there are 2 therapies, but no clear evidence according to EBM-criteria?**



# Summary:

- Early trials → PFOO causes no harm
- Early trials → strong signs that PFOO is superior to antiplatelets
- CLOSE, REDUCE → PFOO superior to antiplatelets within 3y
  - The question for the future: PFOO or life-long oral anticoagulation?
- DEFENSE-PFOO → PFOO superior to medTx in high-risk PFO's
- The future: more AF

**PFO closure for secondary prevention ✓**



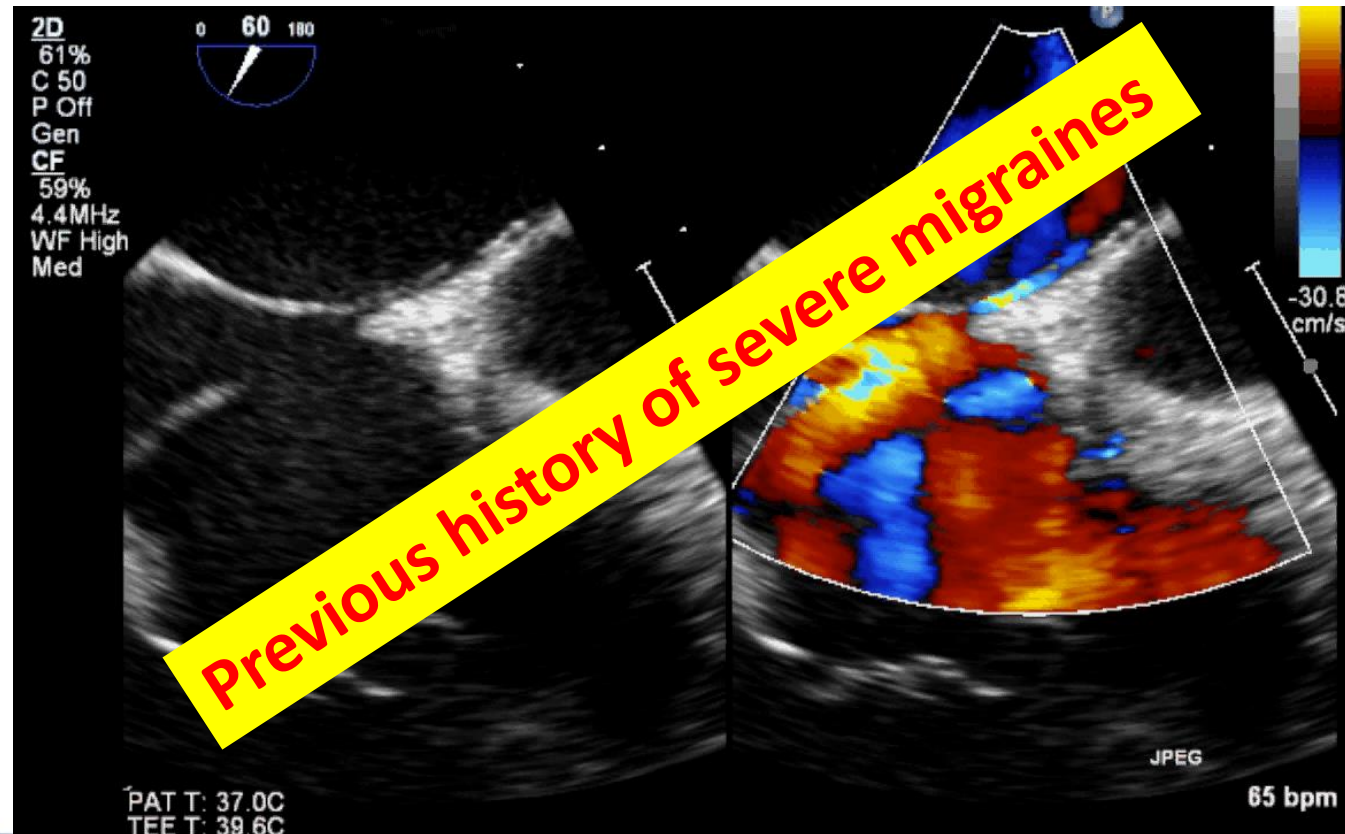
# Is there a role for PFOO beyond secondary prevention?

**What do we do, when there are 2 therapies, but no clear evidence according to EBM-criteria?**

- How many patients suffered a stroke, because PFOO was denied until 2017?
- How can we do better in preventing strokes?

# New Years Eve 2013

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# Primary prevention?

Maybe worth a thought?



Meier, Nietlispach, EHJ 2018



# Thank you!



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HIRSLANDEN



KLINIK IM PARK



TVT2019  
STRUCTURAL HEART SUMMIT



Cardiovascular  
Research Foundation